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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,650	02/09/2004	Doug Hui Huang	034827-1502	3526

30542 7590 09/06/2006

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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 09/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/775,650	HUANG ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-27* is/are rejected.

7)☒ Claim(s) *24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/4/04 & 4/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III, claims 24-27 and SEQ ID Numbers 13 and 14, in the reply filed on August 11, 2006 is acknowledged. The traversal is on the ground(s) that a) the search of all of the recited sequences would provide a clear indication of the state of the relevant art; and b) that the search of all sequences would not impose a serious search burden because database computer searching of nucleic acid sequences is routine and quick. (page 12, 5th paragraph). This is not found persuasive for the following reasons.

The examiner respectfully disagrees with Applicants' remark stating that the database computer searching of nucleic acid sequences is routine and quick. The protocol which the Office implements for a search of given SEQ ID Number is unlike the searches that are routinely done on, for example, BLAST.

For a given SEQ ID Number, a group of databases which include all patent databases, all commercial databases, all published databases and all non-published, but pending (i.e., interference) databases must be search. For the Office to conduct searches multiple SEQ ID Numbers for all of these databases would result in an enormous burden on the Office, as well as to the examiner of record for reviewing all of the outputted search results. In addition, Applicants' characterization that the results from a sequence search would necessarily provide the state of the relevant art is not entirely correct. There are a plurality of biological assays involving nucleic acids. For example, a portion of nucleic acid could be employed not only in diagnosis regarding its presence/absence, but also for mutations (embracing insertion, deletion, polymorphism, haplotypes, heterozygosity, hemizygosity, homozygosity), as well as therapies involving the same portion of genes, etc.

Clearly, the sequence searches and the review of such results would provide a vast amount of results involving divergent aspects of biotechnology, all of which would be associated with the same portion of a gene.

Hence, it is maintained that the searching of multiple groups as identified would impose an undue search burden and the restriction is maintained.

The requirement is still deemed proper and is therefore made FINAL.

Applicants are invited to keep the withdrawn claims pending, however, in case an allowable subject matter may be found during prosecution, so as to possibly rejoin some of the withdrawn claims.

Claims 1-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on August 11, 2006.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

The parent application 10/659,582 to which instant application claim priority under 35 U.S.C. 120, contains proper written support for SEQ ID Numbers 13 and 14 (examined invention), and thus priority is accorded.

The effective filing date of the present application is September 9, 2003 therefore.

Drawings

The drawing received on February 9, 2004 is acceptable.

Information Disclosure Statement

The IDS received on May 4, 2004 and April 10, 2006 are acknowledged.

Signed copy of their PTO-1449 are enclosed herewith.

Claim Objections

Claim 24 is objected to for not being drawn to the elected invention:

Claim 24 is drawn to a kit comprising one or more pairs of nucleic acid primer selected from a Markush group of SEQ ID Numbers, but the claim does not require the elected embodiment – SEQ ID Numbers 13 and 14.

Amending the claim to recite that said one or more pairs of nucleic acid primer(s) include SEQ ID Numbers 13 and 14 would overcome this objection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wall et al. (Human Mutations, 1995, vol. 5, pages 333-338; IDS reference) in view of Shuber et al. (U.S. Patent

No. 6,818,404, issued November 16, 2004, filed April 11, 2002, priority October 23, 1997; IDS reference).

Wall et al. disclose a method of amplifying know mutations on known cystic fibrosis gene, and in particular, 31 mutations found on exons 3, 4, 5, 7, 9, 10, 11, 12, 13A, 17B, 19, 14B, 21, and intron 19 (page 333, 2nd column, 1st paragraph; Table 1) via use of primer sequences flanking the desired mutations.

It is noted that SEQ ID Numbers 13 and 14 flank the mutation, N1303K (see instant specification page 33) found on exon 21. This exact mutation is detected by Wall et al. (Table 1).

Wall et al. employ primers flanking the mutations R117H, 621+1, and Y122X were found on exon 4. These exact mutations are flanked by the primer of SEQ ID Numbers 3 and 4 (see instant specification page 19 and 20).

Wall et al. employ primers flanking mutation 3846+10 kb found on intron 19 (Table 1, page 335). This exact mutation is flanked by the primer of SEQ ID Numbers 5 and 6 (see instant specification page 32, top).

Wall et al. employ primers flanking mutations R334W, R347P, and R347H on exon 7 (Table 1, page 335). These exact mutations are flanked by the primer of SEQ ID Numbers 7 and 8 (see instant specification pages 21 and 22).

Wall et al. employ primers flanking mutation 1898+1 for exon 12. This mutation is flanked by the primer of SEQ ID Numbers 9 and 10 (see instant specification page 27).

Wall et al. employ primers flanking mutation 2789+5 on exon 14b (Table 1). This mutation is flanked by the primer of SEQ ID Numbers 11 and 12 (see instant specification page 29).

Wall et al. employ primers flanking mutations G551D, G542X, S549R(T-G), 1717-1, R560T, R553X, S549N on exon 11 (Table 1). These mutations are flanked by the primer of SEQ ID Numbers 15 and 16 (see instant specification pages 24 and 25).

Wall et al. employ primers flanking mutations W1282X and 3905insT on exon 20 (Table 1). These mutations are flanked by the primer of SEQ ID Numbers 17 and 18 (see instant specification page 32).

Wall et al. employ primers flanking mutation G85E on exon 3 (Table 1). This mutation is flanked by the primer of SEQ ID Numbers 19 and 20 (see instant specification page 18).

Wall et al. employ primers flanking mutation A455E on exon 9 (Table 1). This mutation is flanked by the primer of SEQ ID Numbers 21 and 22 (see instant specification page 23).

Wall et al. employ primers flanking mutation 2184delA on exon 13 (Table 1). This mutation is flanked by the primer of SEQ ID Numbers 23 and 24 (see instant specification page 28).

Wall et al. employ primers flanking mutations ΔF508, ΔI507, Q493X, and V520F on exon 10 (Table 1). These mutations are flanked by the primer of SEQ ID Numbers 27 and 28 (see instant specification page 24).

Wall et al. employ primers flanking mutations R1162X, 3659delC, and 3849+4(A-G) on exon 19 (Table 1). These mutations are flanked by the primer of SEQ ID Numbers 29 and 30 (see instant specification page 31).

Wall et al. employ primers flanking mutation 711+1 on exon 5 (Table 1). This mutation is flanked by the primer of SEQ ID Numbers 31 and 32 (see instant specification page 21).

In sum, Wall et al. disclose a primer set comprising 14 pairs of primers which flank the above discussed mutations.

Wall et al. do no employ the universal primer sequence (GCGGTCCCAAAAGGGTCAGT) appended at the end of the primer sequences which are specific for the nucleic acid sequence flanking the mutations found on CFTR gene.

Shuber et al. disclose a method of amplifying a known region employing the universal sequence (described above) appended at the end of the primers (column 7, lines 57-61).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Wall et al., and Shuber et al. thereby arriving at the invention as claimed for the following reasons.

Wall et al. disclose a well-known method of assaying for mutations found on a gene implicated with a particular phenotype, in the present case, cystic fibrosis. The artisans, in particular devise a plurality of primer pairs which flank a plurality of mutations found across a plurality of exons and intron found on CFTR gene.

Hence, given the fact that the entire sequence of the CFTR gene was known and available to one of ordinary skill in the art at the time the invention was made, coupled with the motivation to assay for mutations found on all exons/intron of this gene (as provided for by Wall et al.) which may implicate an individual with cystic fibrosis, the mutations of which are flanked by the primers of the instant claims, one of ordinary skill in the art at the time the invention was made would have been motivated to employ any primer pairs which flank the known and disclosed mutations of Wall et al. so as to amplify and detect the presence or absence of mutation in a clinical/research samples. In other words, given that the gene is known and the mutation is known, it would be well within the purview of an ordinarily skilled artisan to design any primer pairs which surround the known mutations.

In addition, one of ordinary skill in the art at the time the invention was made would have been also motivated to append the universal priming sequence of Shuber et al. to the ends of the primer for the benefit of increasing the specificity of the amplification of the target nucleic acids in the sample.

Shuber et al. achieve this benefit by conducting an initial amplification of the target nucleic acids with a primer pair, each of which comprising a portion which is complementary to the target nucleic acid, and a portion which is not complementary to target nucleic acid, wherein the latter portion is high in G-C content (column 3, lines 31-46).

Following the first amplification cycle, the subsequent amplification is achieved by second primer pairs which are specific for the latter portions, which requires a higher melting temperatures, providing for more stringent amplification, resulting in lesser background noise in the amplification/detection method (column 3, lines 8-30).

Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to employ the teachings of Wall et al., so as to arrive at a primer pair which flanks know mutations on CFTR gene, wherein said ordinarily skilled artisan would have been motivated to employ the appended, high G-C content, priming sequences to the ends of the primers (as provided for by Shuber et al.), for the benefit of achieving specific and more stringent amplification of the target sequences with a reasonable expectation of success.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wall et al. (Human Mutations, 1995, vol. 5, pages 333-338; IDS reference) in view of Shuber et al. (U.S. Patent No. 6,818,404, issued November 16, 2004, filed April 11, 2002, priority October 23, 1997; IDS

reference) as applied to claims 24-26 above, and further in view of Claustres et al. (Human Mutations 2000, vol. 16, pages 143-156).

The teachings of Wall et al. and Shuber et al. have already been discussed above.

Neither Wall et al. nor Shuber et al. disclose a mutation found on exon 16 of CFTR gene.

Claustres et al. disclose a mutation found on exon 16 of CFTR gene, wherein the mutation is D993Y, 3120G->A, and 3120+1G->A (Figure 1 on page 147). These mutations are flanked by the primer of SEQ ID Numbers 25 and 26 (see instant specification page 30).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to arrive at a collection of primer pairs which include the mutations disclosed by of Claustres et al., that is, mutations found on exon 16, thereby arriving at the claimed invention for the benefit of arriving at a collection of primer sets which is capable of identifying a collection of mutations found on CFTR gene which may be used for diagnosing cystic fibrosis in an individual.

As the desire to detect mutations associated with cystic fibrosis had been well-established, one of ordinary skill in the art at the time the invention was made would have been naturally led and motivated to arrive at a kit which comprises primer pairs which represent a comprehensive collection of known mutations found on cystic fibrosis with a reasonable expectation of success.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot

guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Young J. Kim
Primary Examiner
Art Unit 1637
9/1/2006

YOUNG J. KIM
PRIMARY EXAMINER

YJK